

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence as set forth in SEQ ID NO: 7 or 9;
- (b) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 8 or 10;
- (c) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of (a) or (b), wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10; and
- (d) a nucleotide sequence complementary to any of (a)-(c).

2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence encoding a polypeptide that is at least about 70, percent identical to the polypeptide as set forth in SEQ ID NO: 8 or 10, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;
- (b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 7 or 9, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;
- (c) a nucleotide sequence of SEQ ID NO: 7 or 9; (a); or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;
- (d) a nucleotide sequence of SEQ ID NO: 7 or 9, or (a)-(c) comprising a fragment of at least about 16 nucleotides;
- (e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(d), wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10; and
- (f) a nucleotide sequence complementary to any of (a)-(c).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 or 10 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 or 10 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 or 10 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(d) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 or 10 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(e) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 or 10 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(f) a nucleotide sequence of (a)-(e) comprising a fragment of at least about 16 nucleotides;

(g) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(f), wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10; and

(h) a nucleotide sequence complementary to any of (a)-(e).

4. A vector comprising the nucleic acid molecule of claims 1, 2, or 3.

5. A host cell comprising the vector of claim 4.

6. The host cell of claim 5 that is a eukaryotic cell.

7. The host cell of claim 5 that is a prokaryotic cell.
8. A process of producing a tmst2-receptor polypeptide comprising culturing the host cell of claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.
9. A polypeptide produced by the process of claim 8.
10. The process of claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native tmst2-receptor polypeptide operatively linked to the DNA encoding the tmst2-receptor polypeptide.
11. The isolated nucleic acid molecule according to claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.
12. A process for identifying candidate inhibitors of tmst2-receptor polypeptide activity or production comprising exposing a cell according to claims 5, 6, or 7 to the candidate inhibitors, and measuring tmst2-receptor polypeptide activity or production in said cell, comparing activity or production in the presence and absence of the candidate.
13. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 8 or 10.
14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:
 - (a) the mature amino acid sequence as set forth in SEQ ID NO: 8 or 10, comprising a mature amino terminus at residue 1, optionally further comprising an amino-terminal methionine;

(b) an amino acid sequence for an ortholog of SEQ ID NO: 8 or 10, wherein the encoded polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(c) an amino acid sequence that is at least about 70 percent identical to the amino acid sequence of SEQ ID NO: 8 or 10, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(d) a fragment of the amino acid sequence set forth in SEQ ID NO: 8 or 10 comprising at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(e) an amino acid sequence for an allelic variant or splice variant of either the amino acid sequence as set forth in SEQ ID NO: 8 or 10, or at least one of (a)-(c) wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10.

15. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as set forth in SEQ ID NO: 8 or 10 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(b) the amino acid sequence as set forth in SEQ ID NO: 8 or 10 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(c) the amino acid sequence as set forth in SEQ ID NO: 8 or 10 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10;

(d) the amino acid sequence as set forth in SEQ ID NO: 8 or 10 which has a C- and/or N-terminal truncation, wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10; and

(e) the amino acid sequence as set forth in SEQ ID NO: 8 or 10, with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation,

wherein the polypeptide has an activity of the polypeptide as set forth in SEQ ID NO: 8 or 10.

16. An isolated polypeptide encoded by the nucleic acid molecule of claims 1, 2, or 3.

17. The isolated polypeptide according to claim 14 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

18. An antibody produced by immunizing an animal with a peptide comprising an amino acid sequence of SEQ ID NO: 8 or 10.

19. An antibody or fragment thereof that specifically binds the polypeptide of claims 13, 14, or 15.

20. The antibody of claim 19 that is a monoclonal antibody.

21. A hybridoma that produces a monoclonal antibody that binds to a peptide comprising an amino acid sequence of SEQ ID NO: 8 or 10.

22. A method of detecting or quantitating the amount of tmst2-receptor polypeptide using the anti-tmst2-receptor antibody or fragment of claims 18, 19, or 20.

23. A selective binding agent or fragment thereof that specifically binds at least one polypeptide wherein said polypeptide comprises the amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as set forth in SEQ ID NO: 8 or 10;
- (b) a fragment of the amino acid sequence set forth in at least one of SEQ

ID NO: 8 or 10; and

(c) a naturally occurring variant of (a) or (b).

24. The selective binding agent of claim 23 that is an antibody or fragment thereof.
25. The selective binding agent of claim 23 that is a humanized antibody.
26. The selective binding agent of claim 23 that is a human antibody or fragment thereof.
27. The selective binding agent of claim 23 that is a polyclonal antibody or fragment thereof.
28. The selective binding agent claim 23 that is a monoclonal antibody or fragment thereof.
29. The selective binding agent of claim 23 that is a chimeric antibody or fragment thereof.
30. The selective binding agent of claim 23 that is a CDR-grafted antibody or fragment thereof.
31. The selective binding agent of claim 23 that is an antiidiotypic antibody or fragment thereof.
32. The selective binding agent of claim 23 which is a variable region fragment.
33. The variable region fragment of claim 32 which is a Fab or a Fab' fragment.
34. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NO: 8 or 10.

35. The selective binding agent of claim 23 which is bound to a detectable label.
36. The selective binding agent of claim 23 which antagonizes tmst2-receptor polypeptide biological activity.
37. A method for treating, preventing, or ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to claim 23.
38. A selective binding agent produced by immunizing an animal with a polypeptide comprising an amino acid sequence of SEQ ID NO: 8 or 10.
39. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to claims 1, 2, or 3.
40. A composition comprising the polypeptide of claims 13, 14, or 15 and a pharmaceutically acceptable formulation agent.
41. The composition of claim 40 wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.
42. The composition of claim 40 wherein the polypeptide comprises the mature amino acid sequence as set forth in SEQ ID NO: 8 or 10.
43. A polypeptide comprising a derivative of the polypeptide of claims 13, 14, or 15.
44. The polypeptide of claim 43 which is covalently modified with a water-soluble polymer.

45. The polypeptide of claim 44 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.
46. A composition comprising a nucleic acid molecule of claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.
47. A composition of claim 46 wherein said nucleic acid molecule is contained in a viral vector.
48. A viral vector comprising a nucleic acid molecule of claims 1, 2, or 3.
49. A fusion polypeptide comprising the polypeptide of claims 13, 14, or 15 fused to a heterologous amino acid sequence.
50. The fusion polypeptide of claim 49 wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.
51. A method for treating, preventing or ameliorating a medical condition in a mammal resulting from decreased levels of tmst2-receptor polypeptide comprising administering to a patient the polypeptide of claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid of claims 1, 2, or 3 to said mammal.
52. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject caused by or resulting from abnormal levels of tmst2-receptor polypeptide comprising:
- (a) determining the presence or amount of expression of the polypeptide of claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid molecule of claims 1, 2, or 3 in a sample; and

(b) comparing the level of tmst2-receptor polypeptide in a biological, tissue or cellular sample from normal subjects or the subject at an earlier time, wherein susceptibility to a pathological condition is based on the presence or amount of expression of the polypeptide.

53. A device, comprising:

(a) a membrane suitable for implantation; and

(b) cells encapsulated within said membrane, wherein said cells secrete a protein of claims 13, 14, or 15, and wherein said membrane is permeable to said protein and impermeable to materials detrimental to said cells.

54. A device, comprising:

(a) a membrane suitable for implantation; and

(b) the tmst2-receptor polypeptide encapsulated within said membrane, wherein said membrane is permeable to the polypeptide.

55. A method of identifying a compound which binds to a polypeptide comprising:

(a) contacting the polypeptide of claims 13, 14, or 15 with a compound; and

(b) determining the extent of binding of the polypeptide to the compound.

56. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of claims 1, 2, or 3.

57. A transgenic non-human mammal comprising the nucleic acid molecule of claims 1, 2, or 3.

58. A diagnostic reagent comprising a detectably labeled polynucleotide encoding the amino acid sequence set out in SEQ ID NO: 8 or 10; or a fragment, variant or homolog thereof including allelic variants and spliced variants thereof.

59. The diagnostic reagent of claim 58, wherein said labeled polynucleotide is a first-strand cDNA.

60. A method for determine the presence of tmst2-receptor nucleic acids in a biological sample comprising the steps of:

- (a) providing a biological sample suspected of containing tmst2-receptornucleic acids;
- (b) contacting the biological sample with a diagnostic reagent according to claim 59 under conditions wherein the diagnostic reagent will hybridize with tmst2-receptornucleic acids contained in said biological sample;
- (c) detecting hybridization between tmst2-receptornucleic acid in the biological sample and the diagnostic reagent; and
- (d) comparing the level of hybridization between the biological sample and diagnostic reagent with the level of hybridization between a known concentration of tmst2-receptor nucleic acid and the diagnostic reagent.

61. A method for detecting the presence of tmst2-receptor nucleic acids in a tissue or cellular sample comprising the steps of:

- (a) providing a tissue or cellular sample suspected of containing tmst2-receptor nucleic acids;
- (b) contacting the tissue or cellular sample with a diagnostic reagent according to claim 59 under conditions wherein the diagnostic reagent will hybridize with tmst2-receptor nucleic acids;
- (c) detecting hybridization between tmst2-receptor nucleic acid in the tissue or cellular sample and the diagnostic reagent; and
- (d) comparing the level of hybridization between the tissue or cellular sample and diagnostic reagent with the level of hybridization between a known concentration of tmst2-receptor nucleic acid and the diagnostic reagent.

62. The method of claim 59 wherein said polynucleotide molecule is DNA.

63. The method of claim 59 wherein said polynucleotide molecule is RNA.